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**Effects of Human Interferon and
2',5'-Oligoadenylates on Protein Synthesis in
Plant Tissues**

18400166 Moscow DOKLADY AKADEMII NAUK
SSSR in Russian Vol 297, No 4, Dec 87 (manuscript
received 17 Jul 87) pp 1018-1021

[Article by I.B. Kaplan, S.I. Malysenko, A.B. Fedina,
M.E. Talyanskiy, M.Ya. Karpeyskiy, V.I. Ogarkov (dec)
and I.G. Atabekov, full member, All-Union Academy of
Agricultural Sciences imeni Lenin, Moscow State Uni-
versity; Institutes of Plant Physiology imeni K.A. Timir-
yazev and of Molecular Biology, USSR Academy of
Sciences; All-Union Scientific Research Institute of Bio-
technology, Moscow]

[Abstract] Trials were conducted with tobacco and wheat
plants to determine whether recombinant human leu-
kocytic interferon (INF) and one of its mediators in
animal cells, 2',5'-oligoadenylates (2-5A), are capable of
inducing pathogenesis-related (PR) and heat shock (HS)

proteins. Polyacrylamide gel analysis of the protein
patterns in tobacco leaves (*N. tabacum* var. Samsun NN)
demonstrated that treatment of the leaves with 0.1 U/ml
INF resulted in the induction of three PR proteins that
were also induced by exposure of the leaves to TMV.
However, rubbing the tobacco leaves with 100 U/ml INF
was less effective, resulting in the synthesis of only one
PR protein. At concentrations of 10^{-6} to 10^{-8} M, 2-5A
also led to the synthesis of the same three PR proteins. In
addition, INF was also effective in inducing the synthesis
of two HS proteins in wheat leaves after 24 h of exposure
at 23°C. Analogous results were obtained with 2-5A.
These observations suggest that INF and 2-5A may
function to create a stressful situation in plants leading
to synthesis of protective proteins, in this case PR in
tobacco and HS in wheat under the experimental condi-
tions employed. The extent to which these findings are
related to putative 'phytointerferon' remain to be eluci-
dated. Figures 2; references 15: 2 Russian, 13 Western.

12172/9604

**Monoclonal Antibodies Against
Bacteriorhodopsin: Photoinduced Crosslinking and
Effects on Combination of Retinal With
Bacterioopsin**

18400193 Moscow *BIOLOGICHESKIYE MEMBRANY
in Russian Vol 4, No 11, Nov 87 (manuscript received
27 May 87) pp 1136-1141*

[Article by A.B. Kuryatov, V.V. Ulyatin and V.I. Tsetlin,
Institute of Bioorganic Chemistry imeni M.M. Shemya-
kin, USSR Academy of Sciences, Moscow]

[Abstract] A study was designed to determine whether monoclonal antibodies (MCAb) against bacteriorhodopsin bind to the external or cytoplasmic side of the Halobacterium halobium purple membrane. The MCAbs [Vtyurin, I.Yu. et al., Biol. Membrany, 1(11):1161-1170, 1984], designated H5F3, ID2G1, H5E5, and A14H3, were tested for their effects on bacteriorhodopsin regeneration and for the formation of photoinduced crosslinks with derivatized bacteriorhodopsin. The fluorescent photoactive derivatives were obtained by carbodiimide-mediated reaction of the 232-248 C-terminal fragment of retinylbacterioopsin with p-azidobenzylamine. Resolution on HPLC and fluorescent monitoring of elution peaks demonstrated that only MCAbs H5E5 and A14H3 formed covalent complexes with the labeled derivatives, indicating localization of the antibodies on the cytoplasmic face of the purple membrane in accordance with the disposition of the C-terminus. The rate constants for bacteriorhodopsin regeneration were slowed by a factor of 1.5- to 2.5-fold by the MCAbs, with H5E5 inducing the most pronounced reduction. The latter effects were attributed to the fact that H5E5 is specific for the antigenic determinant encompassing Asp^{35/38} and Phe⁴², and screened moieties Lys⁴⁰ and Lys⁴¹ from Schiff base formation with retinal. Figures 3; references 14: 4 Russian, 10 Western.

12172/9604

**Synthesis of Active Luciferase of Firefly Luciola
Mingrelica and Its Stability in Oocytes of Frog
Xenopus Laevis**

18400167a Moscow *DOKLADY AKADEMII NAUK
SSSR in Russian Vol 297, No 4, Dec 87 (manuscript
received 7 Apr 87) pp 999-1002*

[Article by G.D. Kutuzova, Ye.A. Skripkin, N.I. Tarasova, N.N. Ugarova and USSR Academy of Sciences corresponding members A.A. Bogdanov and I.V. Berezin (dec), Moscow State University imeni M.V. Lomonosov]

[Abstract] A study was conducted on the kinetics of synthesis of luciferase of the firefly *Luciola mingrelica* in the oocytes of the frog *Xenopus laevis*, to further test the oocytes as a system for translating mRNA from various sources. The oocytes were microinjected with 40 nL of an aqueous preparation of *L. mingrelica* mRNA (poly(A⁺)RNA; 1 mg/ml) and incubated at 18°C in

Ringer's solution. Testing of the oocyte homogenates demonstrated that, within 3 h, luciferase activity was present, reaching a peak in 24 h. Activity persisted in the oocytes for over a week, decreasing at that time to 10 percent of the maximum luciferase activity. Additional experiments showed that translation of the mRNA was 1000-fold more efficient in the oocytes than in reticulocyte lysates. At the point of maximum activity (24 h) the oocytes contained ca. 10^{-14} moles of luciferase, equivalent to a 10^{-8} M concentration. Reduction of luciferase activity in the oocytes was attributed to concomitant synthesis of firefly proteases, and presumably greater structural lability of luciferase synthesized within the oocytes. The simplicity and sensitivity of the bioluminescent method, with a limit of detection of 10^{-18} moles, demonstrate the utility of using the firefly mRNA as a marker in studying protein biosynthesis. Figures 3; references 12: 1 Russian, 11 Western.

12172/9604

**Chimeric Regulatory Peptides as Instruments for
Analysis of Their Functions**

18400167b Moscow *DOKLADY AKADEMII NAUK
SSSR in Russian Vol 297, No 5, Dec 87 (manuscript
received 12 May 87) pp 1264-1267*

[Article by Ye.P. Kharkchenko, T.V. Sokolova, V.N. Kalikhevich, K.I. Shestak, Z.A. Ardemasova and A.Ya. Bagrov, Institute of Evolutionary Physiology and Biochemistry imeni I.M. Sechenov, USSR Academy of Sciences, Leningrad]

[Abstract] In order to better define the structural parameters underlying the functional characteristics of various regulatory peptides, studies were conducted with hybrid molecules prepared by joining leu-enkephalin and neurotensin components into a chimeric peptide. The peptides under investigation consisted of leu-enkephalin on the N-side and the 9-13 fragment of neurotensin on the C-end (Tyr-Gly-Gly-Phe-Leu-Arg-Pro-Tyr-Ile-Leu), designated iefbin I, and a hexapeptide Tyr-Arg-Pro-Tyr-Ile-Leu (iefbin II) representing a pentaneurotensin with a Tyr moiety on the N-terminus. Iefbin I and II and pentaneurotensin (9-13) in concentrations of 10^{-8} to 10^{-9} M increased the muscle tone of isolated guinea pig ileum; addition of naloxone was without effect on the changes induced by these peptides. Intracisternal injection of these peptides in mice in a concentration of 0.5×10^{-8} M (5 μ L), as well as leu-enkephalin, showed an analgesic effect within 5 min. Iefbin I, II, and pentaneurotensin were effective in both the tail compression and hot-plate tests, whereas leu-enkephalin was effective only in the latter test. The effects were dose-dependent and overcome by naloxone administration. These observations point to the predominance of the physiological effects of the neurotensin component in the chimeric peptides, with the naloxone findings implicating reaction with opioid receptors in certain situations. Figures 1; references 12: 5 Russian, 7 Western.

12172/9604

Synthesis and Properties of Acyclic Analogs of Ribavirin

18400167c Moscow *BIOORGANICHESKAYA KHIMIYA* in Russian Vol 13, No 9, Sep 87 (manuscript received 6 Jan 87) pp 1240-1244

[Article by T.L. Tsilevich, S.V. Kochetkova, I.L. Shchavaleva, I.P. Smirnov, B.P. Gottikh and V.L. Florentyev, Institute of Molecular Biology, USSR Academy of Sciences, Moscow]

[Abstract] In order to further expand the armamentarium of broad spectrum antivirals, a series of acyclic analogs of ribavirin was synthesized. The synthetic approach consisted of condensation of trimethylsilylated 3-ethoxy-carbonyl-1,2,4-triazole with alkylating agents

in the presence of SnCl_4 in acetonitrile, followed by treatment with methanolic ammonia. The structures of the analogs were confirmed by PMR and UV spectroscopy data, showing the following analogs with cleaved $\text{C3}'\text{-C4}'$ bond in the furanose ring: 1-(1-hydroxy-4-oxahex-3-yl)-1,2,4-triazole-3-carboxamide, 1-(1-chloro-4-oxahex-3-yl)-1,2,4-triazole-3-carboxamide, 1-(1,2-dihydroxy-4-oxahex-3-yl)-1,2,4-triazole-3-carboxamide, 1-(1,6-dihydroxy-4-oxahex-3-yl)-1,2,4-triazole-3-carboxamide, 1-(1-chloro-6-hydroxy-4-oxahex-3-yl)-1,2,4-triazole-3-carboxamide, and 1-(1,2,6-trihydroxy-4-oxahex-3-yl)-1,2,4-triazole-3-carboxamide. The starting compound for the alkylating agents was acrolein, converted to the desired acetal forms. References 6: 5 Russian, 1 Western.

12172/9604

**Diffusion Processes and Leading Centers in
Concentration-Active Media With First Order
Boundary Conditions**

18400190 Moscow BIOFIZIKA in Russian

*Vol 32, No 6, Nov-Dec 87 (manuscript received 3 Dec
86) pp 1038-1045*

[Article by A.N. Zaikin, Institute of Biological Physics,
USSR Academy of Sciences, Pushchino, Moscow
Oblast]

[Abstract] A mathematical analysis is undertaken of oscillating chemical reactions with first-order boundary conditions, resulting in periodic propagation of concentrations waves. The reaction commences at a given point (leading center) and disseminates in the form of a circular wave. Waves from different leading centers collide with mutual annihilation taking place, with the point of collision moving towards the leading center with the longer period. Eventually, the leading center with the highest frequency synchronizes the entire space. The

nature of a leading center in a thin layer of active medium remains enigmatic, with considerable difficulties being encountered in attempts at modeling leading centers with different periods. A new approach to modeling leading centers takes into consideration the fact that geometric factors may be of key importance in the genesis of a chemical leading center, as well as the nature of the active medium and the boundary or physical limiting conditions. It can be shown mathematically that, in chemical and biochemical media, diffusion may serve not only to facilitate contact among the elements of the medium in question, but, in first-order boundary conditions, may replace certain kinetic stages in the process. Such a replacement favors retention of isothermicity, and the other reactions may proceed under milder conditions of temperature or pH, for example. Such reasoning has been used to model impulse propagation in myocardium. Figures 9; references 10: 5 Russian, 5 Western.

12172/9604

Optimization of Batch Cultivation of Biomass

18400071a Kiev DOKLADY AKADEMII NAUK
UKRAINSKOY SSR, SERIYA B:
GEOLOGICHESKIYE, KHIMICHESKIYE I
BIOLOGICHESKIYE NAUKI in Russian
No 8, Aug 87 (manuscript received 23 Jan 87) pp 73-76

[Article by Ye.G. Kosman and I.P. Sirenko, Institute of Botany, Ukrainian SSR Academy of Sciences, Kiev]

[Abstract] Detailed mathematical analysis was conducted on the optimization of batch cultivation of biomass for attaining optimum economic efficiency in terms of substrate utilization and biomass yield. The entire approach proceeded from the fundamental differential equations relating time, biomass concentration, and substrate concentration: $dx/d\tau = x[(y/(1+y)) - \alpha]$ and $dy/d\tau = -(xy/(1+y))$, where x represents the biomass concentration, y is the substrate concentration, x_0 is the initial biomass concentration, y_0 is the initial substrate concentration, τ is the time, and τ_0 is the starting time; α represents a dimensionless variable with values in the 0 [is less than] α [is less than] 1 range. Lagrangian functions were used to derive maxima providing for a cost-effective process in the case of a homogenous mycelial suspension when the process of cultivation is terminated at a derived maximum time point. Figures 1; references 4 (Russian).

12172/9604

'Turbohypobiosis' of Microbial Cultures in Relation to Hydrodynamic Conditions

18400071b Riga IZVESTIYA AKADEMII NAUK
LATVIYSKOY SSR in Russian No 8, Aug 87
(manuscript received 13 Dec 86) pp 93-96

[Article by M.K. Toma, M.P. Ruklish, U.E. Viyestur, M.A. Rikmanis and Yu.Ya. Vanags, Institute of Microbiology imeni Avgust Kirkhenshteyn, Latvian SSR Academy of Sciences]

[Abstract] The concept of 'turbohypobiosis' is advanced to explain the effects of hydrodynamic factors prevalent in microbial cultures on the physiological and metabolic status of microorganisms. This hypothesis stems from the consideration that shaking is used to introduce oxygen into the culture media to support growth, and that shaker cultures experience considerable hydrodynamic perturbations. Observations on a number of cultures have shown the existence of either narrow or broad turbulence maxima compatible with optimum biosynthetic potential at a given oxygen tension. Thus, in the

case of *Brevibacterium flavum* 22LD optimum aconitase activity was seen with 800 rpm with pO_2 representing 10 percent of saturation value. Furthermore, in the case of *Trichoderma viride* maximum oxygen consumption (Q_{ox}) was observed at ca. 150 rpm, but in the case of *Saccharomyces cerevisiae* and *Polyangium* sp. bacteria a broad diffuse spectrum was evident, with inhibition of metabolic activity above 1000 rpm. The data were consonant with the contention that excessive turbulence created hydrodynamic stress resulting in abatement of metabolic activities, a phenomenon designated by the proposed term 'turbohypobiosis'. Figures 2; references 19: 12 Russian, 7 Western.

12172/9604

Technical Considerations in Production of Natural Phage-Specific Double-Stranded RNA From *Escherichia Coli* Biomass

18400071c Riga IZVESTIYA AKADEMII NAUK
LATVIYSKOY SSR in Russian No 8, Aug 87
(manuscript received 7 Feb 86) pp 121-125

[Article by Yu.B. Umbrashko, P.L. Pildinsh, V.P. Lozha, G.Ya. Feldmane, A.A. Kolesnikov and R.Ya. Karklinsh, Institute of Microbiology imeni Avgust Kirkhenshteyn, Latvian SSR Academy of Sciences]

[Abstract] In view of the demonstrated efficiency of natural double-stranded RNA (dsRNA) as an interferon inducer and its efficacy as an antiviral agent, a pilot-plant study was conducted at the Institute to assess the technical aspects of large-scale dsRNA production. *Escherichia coli* infected with the bacteriophage f2 amber mutant sus-11 were grown in 250 liter fermentors, the biomass harvested by centrifugation and stored at -20°C until use. The chloroform method of Marmur [Marmur, J., J. Mol. Biol., 3(2):208-218, 1961] was used to isolate the nucleic acids. The latter were subsequently treated with selected nucleases to eliminate DNA and single-stranded RNA, followed by immediate addition of bentonite after the incubation to prevent destruction of dsRNA. Then dsRNA was isolated by precipitation with isopropanol (isopropanol:dsRNA = 0.55:1 v/v), followed by centrifugation, and lyophilization. The yield of 2×10^5 dalton dsRNA was on the order of 40 percent of the theoretical concentration, containing 3 percent DNA and 2 percent protein impurities. Intravenous administration to mice of 0.5 mg/kg of the various dsRNA preparations yielded serum interferon titers of 128-512 units/ml. Figures 3; references 14: 11 Russian, 3 Western.

12172/9604

Laser Treatment of Coronary Thrombosis

18400221 Moscow IZVESTIYA in Russian
19 Dec 87 p 3

[Article by S. Tutorskaya: "Beam Treats Vessels"]

[Abstract] Stimulated by a report of Canadian physicians on removing clots from coronary artery by means of a laser beam, the interviewer talked to Director of the Institute of Surgery imeni A.V. Vishnevskiy, USSR Academy of Sciences, Dr M.I. Kuzin and V.I. Burakovskiy, Director of the Institute of Cardiovascular Surgery imeni A.N. Bakulev. Soviet researchers have performed only animal experiments of this type at this time, although clots from lower extremities have been already treated in 60 patients 3 years ago using a helium-neon laser. Researchers at the Vishnevskiy Institute of Surgery are interested in using an excimer laser, which has a milder action in the impulse mode and does not damage tissue.

7813/9604

Effects of CO₂ Laser on Rabbit Blood Vessels

18400173c Moscow VOPROSY NEYROKHIRURGII in Russian No 6, Nov-Dec 87 (manuscript received 31 Aug 86) pp 36-41

[Article by V.I. Ryabenko, L.V. Shishkina and T.M. Vikhert, Institute of Neurosurgery imeni N.N. Burdenko, USSR Academy of Medical Sciences, Moscow]

[Abstract] A histologic study was conducted on chin-chilla rabbits (2-2.5 kg) to assess the effects of a CO₂ laser on the blood vessels, since CO₂ lasers find clinical use as "laser scalpels". The purpose was to define conditions favoring coagulation with a view to preventing hemorrhages. The CO₂ emission (10.6 μ m) was used both in focused (to 1 mm) and defocused (to 9 mm) modes, with the power output varied from 3.7 to 22.7 W. Histologic monitoring of the consequences over a 1 h to 3 month period demonstrated that coagulation of arterial and venous vessels is possible if the diameter does not exceed 0.2-0.3 mm and a focused beam is employed. With a defocused beam, vessels approaching 0.8 mm in diameter may be coagulated. Coagulation of arterial vessels exceeding 1 mm in diameter is impossible in either modality of focusing regardless of energy output as long as blood flow persists. The importance of blood flow velocity was further demonstrated by the fact that veins with a diameter of 3-4 mm were successfully coagulated. Arterial vessels with diameters of 1 mm were successfully coagulated if stasis had been induced. Coagulation with complete obliteration of the lumen involved full-circumference necrosis of the wall. In the absence of coagulation, only a section of the wall may undergo necrosis and, upon further increase in power output, local perforations may occur resulting in hemorrhage. Figures 4; references 8: 5 Russian, 3 Western.

12172/9604

Intragastric Laser Therapy of Ulcers

18400173a Moscow KLINICHESKAYA MEDITSINA in Russian Vol 65, No 10, Oct 87 (manuscript received 18 Nov 86) pp 6-9

[Article by V.B. Matyushichev, A.I. Soldatov and V.V. Titov, Chair of Biochemistry, Leningrad State University; Baltic Basin Central Clinic imeni G.I. Chudnovskiy]

[Abstract] A literature survey was conducted on the advances in endoscopic laser therapy of peptic ulcers, a technique that in many cases has made it possible to avoid operative surgery. The consensus with a variety of endoscopic laser techniques has shown that a healing rate of 50-100 percent is seen within 4 weeks of therapy. The variation in the response is largely due to the different varieties of lasers that have been employed, and their power outputs. Nevertheless, a 2- to 3-fold increase in the cure rate appears real and clinically substantiated. Lasers have been found particularly effective in long-term refractory ulcerative lesions. More often than not healing is accompanied by a modest stellate or linear scar; occasionally, scarring is entirely avoided with complete epithelialization of the site. More recent studies have shown that red light itself from a non-laser source is also quite effective in the management of gastric and duodenal ulcers. Among recent developments in laser therapy has been the use of the yellow-green emission of copper vapor laser (510.6 - 578.2 nm; 6 J dose over 10 sec). One to 4 therapy sessions, at 2-7 day intervals, have resulted in 100 percent cure rates with complete epithelialization. These observations demonstrate that endoscopic laser therapy of gastric and duodenal ulcers represents a novel and effective approach to the management of this type of pathology. References 29: 27 Russian, 2 Western.

12172/9604

Efficacy of Low-Intensity Helium-Neon Laser in Combined Therapy of Gastric and Duodenal Ulcers

18400173b Moscow KLINICHESKAYA MEDITSINA in Russian Vol 65, No 10, Oct 87 (manuscript received 9 Oct 86) pp 66-68

[Article by G.A. Romanov, MONIKI imeni M.F. Vladimirovskiy]

[Abstract] Case studies were analyzed for assessing the therapeutic efficacy of helium-neon laser (632.8 nm) in the management of gastric and duodenal peptic ulcers, in combination with general supportive therapy. The analysis encompassed 86 male and female patients ranging in age from 8 to 76 years. Four patients presented with both gastric and duodenal ulcers. The endoscopic therapy was conducted with either LG-38 or LG-75 laser instrumentation employing conventional fiber optics or single-crystal quartz fiber for light delivery to within 0.5-1.0 cm of the lesion. The course of laser therapy consisted of 3 to 13 applications, 3 times a week. Objective and subjective

improvements in patient status were noted within one to two therapeutic sessions, with accelerated healing eventually terminating in a modest scar or complete epithelialization. In general, the healing process was accelerated 2- to 3-fold in comparison with 100 patients with similar conditions but managed in a conventional manner. A 3-year follow-up showed a 10.4 percent (9 cases)

recurrence rate consisting of superficial defects in the mucosa that were corrected by 2-3 laser treatments. For best results endoscopic monitoring should be accompanied by preventive measures and health-resort treatment. References 8: 7 Russian, 1 Western.

12172/9604

Hyperglycemia in Cancer Therapy

18400222 Kiev *PRAVDA UKRAINY* in Russian
22 Dec 87 p 4

[Article by S. Kalinichev: "No Sensationalism"]

[Abstract] Cancer is viewed as a multiple disease rather than a single entity and therefore a single drug to treat cancer most probably will never be found. A combination of drugs and other therapeutic interventions specifically designed for a given cancer type may

be the proper approach. In the present report hyperthermia coupled with radiation and hyperglycemia is described. These modalities are experimented with at the Institute of Oncological Problems, UkSSR Academy of Sciences. Researchers claim that a combination of hyperthermia and radiation increased the 5-year survival rate of melanoma patients from 12-50 percent to 80 percent.

7813/9604

Microbial Biosynthesis of Porphyrins: Literature Review

18400187a Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian
Vol 23, No 6, Nov-Dec 87 (manuscript received 7 Apr 87) pp 725-739

[Article by V.Ya. Bykhovskiy, N.I. Zaytseva and O.V. Polulyakh, Institute of Biochemistry imeni A.N. Bakh, USSR Academy of Sciences, Moscow]

[Abstract] The growing interest in the various methods of producing porphyrins has largely come from greater appreciation of the applications that these compounds find in various areas of chemistry, medicine, physics, and other areas. In particular, porphyrins have been found to be efficient catalysts in a variety of chemical processes, they have found applications in semiconductors and photosemiconductors, and as labels in fluorescent and luminescent immunoassays, to indicate a few applications. However, the high cost of porphyrins, estimated at \$16,000 or more per gram, has led to investigation of microbial biosynthesis of various porphyrins. One promising approach is based on microbial transformation of chemically synthesized 5-amino-levulinic acid into porphyrins or porphobilinogen, with the latter undergoing condensation to yield a mixture of uroporphyrin isomers. Other methods rely on identification of various microorganisms that are capable of porphyrin biosynthesis, evaluation of the metabolic pathways and their regulatory mechanisms, and delineation of conditions favoring optimum synthesis. Additionally, genetic engineering has been employed for the development of tailor-made systems for porphyrin production and may well be the method of choice for meeting future demands for porphyrin. Figures 2; references 110: 23 Russian, 87 Western.

12172/9604

Chemostatic Cultivation of Plasmid-Bearing *Hansenula polymorpha* DL-1

18400187b Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian
Vol 23, No 6, Nov-Dec 87 (manuscript received 26 Nov 85) pp 779-788

[Article by V.V. Velkov, S.B. Mutafov, A.D. Bazykin and V.K. Yeroshin, Institute of Biochemistry and Physiology of Microorganisms, USSR Academy of Sciences, Pushchino; Institute of Microbiology, Bulgarian Academy of Sciences, Sofia]

[Abstract] A study was conducted on the effects of chemostat cultivation of plasmid pL2-bearing methylotrophic yeast *Hansenula polymorpha* DL-2 on the stability of the plasmid. The vector plasmid pL2 carries a yeast replicon fragment from the mitochondrial DNA of *C. utilis*, as well as marker *leu2* and *arg4* genes from *S.*

cerevisiae. Cultivation of plasmid-bearing *H. polymorpha* on minimal methanol-limited medium lacking leucine designed to eliminate plasmid-free cells resulted in an increase in the plasmid-bearing cells from 40 percent to 80-90 percent. The latter change was attributed to accumulation of stable plasmids with increased stability as a result of spontaneous mutations. Furthermore, all of the cell clones contained plasmids with 35-42 MD DNA, versus a 8.2 MD DNA for the original pL2. Cleavage studies with endonucleases demonstrated that the various plasmids from the different clones differed from one another. Mathematical models were constructed for the process of elimination of plasmid-free cells and accumulation of mutated pL2 plasmids characterized by high stability. The minimum number of plasmid-bearing cells was recorded in ca. the 5-12th cell generations (ca. 10 percent), and the higher levels (80-90 percent) in the 45th and later generations. Figures 3; references 20: 12 Russian, 8 Western.

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Directed Biosynthesis of Macrotetrolides

18400187c Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian
Vol 23, No 6, Nov-Dec 87 (manuscript received 26 Dec 85) pp 800-805

[Article by M.V. Nefedova, A.N. Sverdlova and N.S. Yegorov, Moscow State University]

[Abstract] Studies were conducted on the directed biosynthesis of macrotetrolide homologues by cultures of *Streptomyces chryzomallus* var. *macrotetrolidi*. Addition of organic acid precursors in a concentration of 0.2 percent increased the antibiotic yield and varied its composition. Thus, addition of acetate increased the yield of nonactin to 83.36 percent (68.2 percent control value), diminished the yield of monactin to 16.14 percent from 28.00 percent, and virtually eliminated production of dinactin and trinactin. Addition of propionate or succinate depressed the production of nonactin, but increased the synthesis of the remaining homologues. Addition of various enzyme inhibitors (100-200 µg/ml) was also an effective method for modifying macrotetrolide synthesis. Malonate, an inhibitor of succinate dehydrogenase, depressed the production of nonactin while enhancing the production of monactin and dinactin. A cobalamine analog enhanced the synthesis of nonactin while reducing the synthesis of monactin two-fold, and sulfadimesin, an inhibitor of transmethylation, was virtually without effect on synthesis or composition. References 14: 10 Russian, 4 Western.

12172/9604

Biodegradation of Aniline by *Alcaligenes* Sp. Isolates

18400192a Kiev *MIKROBIOLOGICHESKIY ZHURNAL* in Russian Vol 49, No 6, Nov-Dec 87
(manuscript received 24 Oct 86) pp 38-41

[Article by T.P. Chekhovskaya, V.U. Nikonenko and N.B. Zagornaya, Institute of Colloid Chemistry and Water Chemistry, Ukrainian SSR Academy of Sciences, Kiev]

[Abstract] An *Alcaligenes* sp. isolated from the aniline-polluted soil of the Dneproderzhinsk "Azot" Production Association was tested for its efficiency in degradation of aniline. The culture had a temperature optimum of 28°C, growing best at pH 8.0. The isolate utilized aniline as the sole source of carbon and nitrogen, resulting in complete biodegradation of aniline in concentrations up to 3 g/liter in 48 h. With biodegradation of aniline, the pH of the medium increased due to accumulation of ammonia over the 3 to 24 h span, reaching a plateau at 27 h. *Alcaligenes* cultures maintained on solid media with 1 g/liter aniline were also capable of metabolizing aminophenol and pyrocatechol, which are intermediates of aniline metabolism. However, *Alcaligenes* cultures maintained on beef-peptone agar lacking aniline were incapable of metabolizing these two intermediate products. Figures 3; references 10: 6 Russian, 4 Western.

12172/9604

Hydrophobicity of Paintwork as Factor of Fungal Resistance

18400192b Kiev *MIKROBIOLOGICHESKIY ZHURNAL* in Russian Vol 49, No 6, Nov-Dec 87
(manuscript received 31 Oct 86) pp 49-54

[Article by E.Z. Koval, A.I. Sidorenko and L.P. Sidorenko, Institutes of Microbiology and Virology and of Colloid Chemistry and Water Chemistry, Ukrainian SSR Academy of Sciences, Kiev]

[Abstract] A series of paints designed for metal surfaces were tested for susceptibility to fungal attack to assess their corrosion-inhibiting properties. The resistance of paint coats to growth of *Aspergillus niger*, *A. flavus*, *Penicillium canescens*, and *P. funiculosum* was in direct proportion to their wetting (contact) angles, with the greatest resistance demonstrated by PF-115 black and KhV-518, followed by PF-178 and EF-1118m, and then by ML-12 gray and ML-165 silver. These observations confirmed the fact that paintwork, offering the greatest corrosion protection from fungal attack, shows a high degree of hydrophobicity, with the best results to be expected from paints with a contact angle better than 90°. Primary factors favoring fungal growth on paintwork are high ambient humidity, which leads to condensation on the surface, and sharp temperature drops. Figures 1; references 17: 14 Russian, 3 Western.

12172/9604

Gunshot Fractures of Extremities with Soft Tissue Injury Complicated by Pyogenic Infections

18400177 Moscow *ORTOPEDIYA*,

TRAVMATOLOGIYA I PROTEZIROVANIYE in

Russian No 11, Nov 87 (manuscript received 27 Feb 87)
pp 36-37

[Article by V.A. Khomenko, Central Institute of Traumatology and Orthopedics imeni N.N. Pirogov, Moscow]

[Abstract] An analysis was conducted on the management of 14 cases of gunshot fractures of extremities with extensive soft tissue damage and pyogenic infections. The patients were first seen at the Institute 4 to 26 days after the injury was sustained, following initial treatment elsewhere. The cohort consisted of 11 males and 3 females, ranging in age from 15 to 32 years. Microbiological studies resulted in the isolation of gram-negative

bacteria in 13 cases, with the predominant isolates consisting of *Pseudomonas pyocyaneus* and *Proteus*. In two patients gram negative bacteria were isolated in combination with staphylococci. In three patients, in addition to the gram-negative bacteria, nonsporogenous anaerobes were also identified. The *Pseudomonas* and *Proteus* isolates were found to be resistant to available antibiotics (gentamycin, carbinicillin, cloforan, amikacin, etc.). Consequently, the patients were managed by conventional surgical, orthopedic, tissue sparing, immunogenic and chemotherapeutic measures. In the case of 11 patients, frequent blood transfusions were indicated. After 4 to 12 months of treatment, positive results were obtained in most cases, with one case continuing under treatment. Early plastic surgery of the granulation tissue was felt to be a key factor in preventing osteomyelitis. References 3: 1 Russian, 2 Western.

12172/9604

Bioavailability of Bemtil in Rats

18400205a Moscow *KHIMIKO-FARMAT SEVTI-CHESKIY ZHURNAL in Russian Vol 21, No 11, Nov 87 (manuscript received 8 Jul 86) pp 1288-1291*

[Article by S.S. Boyko, Yu.G. Bobkov and V.P. Zherdev, Institute of Pharmacology, USSR Academy of Medical Sciences, Moscow]

[Abstract] Several methods were used in assessing the bioavailability of the antihypoxic agent bemtil (2-ethyl-mercaptobenzimidazole) in outbred male rats (200-250 g). Aqueous solutions were injected intravenously (10 mg/kg) or administered per os (50 mg/kg), followed by pharmacokinetic monitoring. On intravenous administration the absorption constant was calculated at 1.13 h^{-1} , and the $T_{1/2}$ at 0.614 h^{-1} . The mean residence time after intravenous injection was 1.73 h, and, after per os intake, 2.63 h. In combination with renal excretion, the various measuring methods showed a bioavailability figure from bemtil ranging from 2.12 to 6.37 percent. Bemtil was thus demonstrated to be a compound with low bioavailability, due either to incomplete absorption or rapid presystemic elimination. The rate constant for elimination from the body via urine was 0.644 h^{-1} . Figures 2; references 8: 4 Russian, 4 Western.

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Synthesis and Psychostimulant Activity of Sydnocarb Analogs

18400205b Moscow *KHIMIKO-FARMATSEVTI-CHESKIY ZHURNAL in Russian Vol 21, No 11, Nov 87 (manuscript received 15 Jul 86) pp 1305-1309*

[Article by Z.A. Olovyanishnikova, V.A. Parshin, V.V. Ogorodnikova, M.D. Mashkovskiy and V.G. Yashunskiy, All-Union Scientific Research Institute of Pharmaceutical Chemistry imeni S. Ordzhonikidze; Institute of Biophysics, USSR Ministry of Health, Moscow]

[Abstract] A series of 12 derivatives of sydnocarb (N_6 -phenylcarbamoyl-I, with $I = -3$ -phenylisopropylsydnominine) were synthesized for evaluation of their psychostimulant activities. Synthesis involved reaction of N-nitroso-N-phenylisopropylaminoacetonitrile with various aryl isocyanates, with confirmation of the products provided by PMR, IR, and UV spectroscopies. Evaluation of data obtained with studies on mice, rats, and rabbits showed that the stimulant effects of the 4-substituted derivatives were dependent on both the hydrophobicity and electron-donor characteristics of the substituent, with the dependence expressed by the following equation: $\log(1/C_0) = -1.26\pi^2 + 1.48\pi - 1.13\sigma^0 + 1.17$ ($r = 0.99$), where C_0 is the dose in mM/kg, and π and σ^0 have their usual significance. In particular N_6 -4-tolylcarbamoyl-I, N_6 -4-methyl-3-chlorophenylcarbamoyl-I, N_6 -(4-methoxyphenylcarbamoyl-I, and N_6 -(4-ethoxyphenylcarbamoyl-I) were either equivalent to sydnocarb or exceeded it. The corresponding LD_{50} values in mice for these compounds and sydnocarb were 810, 400, 460, 535, and 1000 mg/kg. References 7 (Russian).

12172/9604

Physicochemical Aspects of Structure-Activity Relationships

18400205c Moscow *KHIMIKO-FARMAT SEVTI-CHESKIY ZHURNAL in Russian Vol 21, No 11, Nov 87 (manuscript received 29 Sep 86) pp 1338-1341*

[Article by O.A. Rayevskiy and A.M. Sapegin, Institute of Physiologically Active Substances, USSR Academy of Sciences, Moscow Oblast]

[Abstract] A cursory qualitative discussion is presented of the increasingly greater emphasis being placed on the mathematical aspects of quantitative structure-activity relationships (QSAR). Analysis of extensive data has shown that reliance solely on structural parameters is inadequate for assessing biological activity, and that ligand-receptor interactions must be assessed in terms of electron donor and acceptor parameters. The development of this physicochemical approach has led to a scale based on donor and acceptor (E_s , E_a) factors, encompassing neutral and charged active sites. A comprehensive approach to QSAR involves several steps, consisting of 1) calculation of E_s and E_a of the descriptive components, determination of equilibrium conformations on the basis of molecular mechanics, and selection of common structural elements by means of image recognition. The entire operation may be carried out by means by the use of, for example, a set of TOPLOG programs. References 21: 15 Russian, 6 Western.

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RASTR: Physicochemical Approach to QSAR [Quantitative Structure-Activity Relationships]

18400205d Moscow *KHIMIKO-FARMATSEVTI-CHESKIY ZHURNAL in Russian Vol 21, No 11, Nov 87 (manuscript received 29 Sep 86) pp 1341-1344*

[Article by A.M. Sapegin, A.N. Razdolskiy, V.V. Chistyakov and O.A. Rayevskiy, Institute of Physiologically Active Substances, USSR Academy of Sciences, Moscow Oblast]

[Abstract] Description is provided of a physicochemical method for evaluation of QSAR parameters, which is based on identification of active sites of the molecules under study and definition of qualitative relationships between electronic and spatial characteristics of the active centers and biological activity. Substrate-receptor interactions are assessed in terms of donor-acceptor factors, forming the basis for classification of compounds of interest. Such an approach makes possible the combination of a qualitative classification of compounds in terms of fundamental characteristics with a quantitative assessment of biological activity on the basis of the molecular moieties involved. Thus, the donor-acceptor factors appear as qualitative descriptors of the active centers of the molecule in relation to bioactivity, and as quantitative characteristics when regression models are being constructed. Special programs have been written for the application of the

RASTR [Recognition of Active STRuctures] method to QSAR, consisting of recognition of molecular structures with similar properties and establishment of structure-activity relationships. The complex of RASTR programs has been written in FORTRAN-77 for a NORD-10 minicomputer, using a SINTRAN-III operating system. Figures 1; references 13: 12 Russian, 1 Western.

12172/9604

**Effects of Naloxone on Prolonged
Immobilization-Induced Hypalgesia in Rats**

18400151 Moscow BYULLETEN

*EKSPERIMENTALNOY BIOLOGII I MEDITSINY in
Russian Vol 104, No 9, Sep 87 (manuscript received 16
Mar 86) pp 283-285*

[Article by Ye.A. Kiyatkin, I.Yu. Shamakina and V.N. Zhukov, Department of Neuropharmacology, Institute of Pharmacology, USSR Academy of Medical Sciences, Moscow]

[Abstract] A study was conducted on the effects of naloxone on the nociceptive response of outbred male rats (220-250 g) subjected to 24 h immobilization by being kept in small (15 x 6 x 5.5 cm) cages. Quantitative data on hypalgesia were derived from immersion of the

tails in hot water (60°C) and measurement of the latent period for tail withdrawal. Studies on control rats subjected to immobilization and injected with physiologic saline showed markedly prolonged latent periods, demonstrating stress-induced hypalgesia. The most pronounced increase in hypalgesia was noted within 1 to 6 h of immobilization, with the latent period at 1 h exceeding control latent period by ca. 200 percent. Within 1 h after immobilization was discontinued this group of animals responded with normal latent times. Administration of naloxone (1 mg/kg) in the course of immobilization to an experimental group of rats showed that six naloxone administrations were without effect on the observed results: the responsiveness was identical with that in the control animals. However, after immobilization was terminated the naloxone-treated animals showed aggressiveness and persistence of pronounced hypalgesia for up to 3 h (p is less than 0.001). These observations indicated that stress-induced hypalgesia was not dependent on mechanisms involving endogenous opioids. However, in the post-stress period priming with naloxone had obvious sequelae, the mechanism of action of which remains to be elucidated. Figures 1; references 14: 2 Russian, 12 Western.

12172/9604

**Dispensarization—Mass Health Screening
Program— Requires Precise Diagnostic Methods**
*18400126 Moscow SOVETSKAYA ROSSIYA in
Russian 17 Nov 87 p 1*

[Interview with M. Shtark, professor and head, Interacademic Department of Medical and Biological Cybernetics, Siberian Departments of the USSR Academy of Sciences and of the USSR Academy of Medical Sciences, conducted by M. Komarovskiy, Novosibirsk]

[Abstract] The ineffectiveness of mass screening in the USSR is largely due to the fact that physicians neglect premorbid states and borderline conditions, limiting themselves to routine physical examinations. The problems are further complicated by inadequate diagnostic procedures, lack of modern diagnostic instrumentation,

and an indifferent approach to computer-based data processing. The latter is of particular concern, as computers that are available are often underutilized and simply used for data storage. In general, combination of diagnostic technologies with computerized data processing lags 15 to 20 years in the USSR in comparison with advanced Western countries. An intensive effort to overcome this lag has to be made that requires educational, industrial, and administrative restructuring. Efforts limited to simply copying already outdated Western technology will not do. In the future, an important component of Soviet medical education will consist of training in a new specialty—medical cybernetics—to ensure that medicine is not left behind in the technological revolution.

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